

# **International Conference Diagnosis And Treatment Of Radiation Injury**

**30 August - 3 September 1998, Rotterdam, The Netherlands**

**Sunday August 30**    16:00 - 20:00 Registration open  
                        18:00 - 20:00 Welcome reception

**Monday, August 31**

Welcome, opening address and introduction on behalf of Erasmus  
Universiteit, the Commission of the European Communities, the Department  
of Energy, USA, and the Institut de Protection et de Sûreté Nucléaire,  
Fontenay-aux-Roses, France:  
J. Sinnaeve, F. Hawkins, P. Gourmelon, C.D.A. Verwoerd

## Background and introduction to the meeting G. Wagemaker (Erasmus University Rotterdam, Netherlands)

## Outcome of the previous consensus meetings D. Browne (Fort Detrick, MD, USA)

Chairmen:  
J.D. Tucker (Livermore, CA, USA) & P. Lohman (Leiden, Netherlands)

## Mechanisms of DNA double-strand break repair in mammalian cells J. Essers, R. Tan, S.M.A. Swagemakers, E. Citterio, C.L. Wyman, J. de Wit, J.H.J. Hoeijmakers, R . Kanaar (Rotterdam, Netherlands)

## **Ionizing radiation and the control of the G2 block**

## Growth factors and radiosensitivity Z. Fuks (New York, NY, USA)

13:30 - 15:00

**Session II**  
**Biological Dosimetry**

Chairmen:

V. Stepanenko (Obninsk, Russia) & P. Voisin (Fontenay-aux-Roses, France)

Introduction: Rise and fall of biological dosimetry  
P. Voisin

Application of molecular cytogenetic methods to biological dosimetry  
J.D. Tucker (Livermore, CA, USA)

Absorbed Radiation Dose: Current Status  
A.T. Natarajan (Leiden, Netherlands)

EPR Dosimetry with tooth enamel: Recent achievements in Russia  
V.F. Stepanenko, V.G. Skvortsov, A.I. Ivannikov, A.F. Tsyb, D.D. Tikhounov, L.G. Khamidova, E.A. Kondrachov (Obninsk, Russia)

Development of rapid biodosimetry capability: Use of cytogenetic and molecular biomarkers  
W. Blakely, H. Loats, P.G.S. Prasanna, A.C. Miller, A.E. Director, C.J. Kolanko, R.S. Loftus (Bethesda, MD and Washington DC, USA)

15:30 - 17:00

**Session III**

**Treatment Of The Bone Marrow Syndrome: Growth Factors  
And Ex Vivo Expansion**

Chairmen: D.A. Williams (Indianapolis, IN, USA) & B. Afanasiev (St Petersburg, Russia)

Introduction:

Treatment of the bone marrow syndrome, growth factors and ex vivo expansion  
D.A. Williams

Thrombopoietin: Mechanisms of action and preclinical evaluation in radiation induced myelosuppression  
K.J. Neelis, S.C. C. Hartong, G.R. Thomas, D.L. Eaton, T. Egeland, A.W. Wognum, G. Wagemaker (Rotterdam, NL; South San Francisco, CA, USA; Oslo, Norway)

Activation of gp130 signaling in vivo by the IL-6 super-agonist K-7/D-6 accelerates repopulation of lymphoid organs after irradiation  
D. Frasca, G. Doria, P. Barattini, F. Guidi, AL Salvati, C. Toniatti and G. Ciliberto (Rome, Italy)

New generation growth factors for the treatment of radiation-induced myelosuppression: Chimeric growth factor receptor antagonists  
T.J. MacVittie, A.M. Farese, W.G. Smith, J.P. McKearn (Baltimore, MD and St. Louis MO, USA)

Hematopoietic stem cells: did nature intend for them to divide ex vivo?  
E.F. Srour, A. Gothot, A.C. Ladd, C.M. Traycoff (Indianapolis, IN, USA)

17:00 - 18:00

**Poster session I**

**Topic 1: Molecular and Cellular Events Determining the Outcome  
of Ionizing Radiation Damage**

**Topic 2: Biological Dosimetry**

**Topic 3/4: Diagnosis and Treatment of Hematopoietic Tissue**

**Topic 5: Infections, Sepsis and Immune Reconstitution**

**Topic 6: Diagnosis and Treatment of the Cutaneous Syndrome**

18:00 - 19:00 **Reception In Town Hall**

**Tuesday, September 1**

08:00 - 10:00

**Session IV**

**Treatment Of The Bone Marrow Syndrome : Bone Marrow  
versus Peripheral Blood versus Cord Blood, and Tissue Typing**

Chairmen:

J.H.F. Falkenburg (Leiden, Netherlands) & D. Thierry (Fontenay-aux-Roses, France)

Introduction:

Different sources for hematopoietic stem cells for allogeneic transplantation

J.H.F. Falkenburg, R. Willemze (Leiden, Netherlands)

Repopulating stem cells

G. Wagemaker (Rotterdam, Netherlands)

Results of unrelated cord blood transplants: an analysis of Eurocord registry

E. Gluckman, V. Rocha, F. Garnier, Cl. Chastang (Paris, France)

HLA matching: Strategies in donor selection for bone marrow or stem cells transplantation

G.B. Ferrara (Genoa, Italy)

Peripheral blood stem cells as compared to bone marrow for allogeneic transplantation: Enhanced incidence of graft-versus-host disease?

J.J. Cornelissen (Rotterdam, Netherlands)

10:30 - 12:30

**Session V**  
**Infections, Sepsis, Immune Reconstitution**

**Chairmen:**

T Egeland (Oslo, Norway) & G. Doria (Rome, Italy)

**Introduction:**

Prophylaxis of infections related to stem cell transplantation

T. Egeland (Oslo, Norway)

Immunohematopoietic recovery after allogeneic blood stem cell transplantation

M.R. Bishop (Omaha, NE, USA)

Immune reconstitution after allogeneic stem cell transplantation

J. Storek, MA. Dawson, D.G. Maloney, R.P. Witherspoon (Seattle, WA, USA)

Can injection of donor T cells devoid of reactivity to the recipient promote survival following transplantation of non-genetically MHC compatible hemopoietic stem cells?

A. Fischer (Paris, France)

New generation of anti-endotoxin antibodies: Novel approaches to a vexing problem

A.S. Cross (Baltimore, MD, USA)

13:30 - 15:15

**Parallel Oral Sessions**

**Parallel Session 1:**

**Molecular Events and Biological Dosimetry**

**Chairmen:** A.T. Natarajan & W.F. Blakely

Correlation of levels of mRNA for Interleukin-5 and individual dose of ionizing radiation in Belarusians exposed to radionuclides released during the Chernobyl accident

N. Dainiak, I.V. Karkanitsa, V.A. Ostapenko, V.E. Shevchuk, N. Kruchinsky, G. Shablovsky, Q. Hamid, (Bridgeport, CT, USA; Gomel, Belarus)

Cytogenetic features of leukemias observed in patients living in the Chernobyl fallout - contamination areas

E.V. Domracheva, E.A. Asseeva, L.V. Diachenko, T.N. Obuchova, J.V. Olshanskaya, A.I. Vorobiov (Moscow, Russia)

Human lymphocyte micronucleus assay as an indicator of radiation injury

Gy. Horváth, I. Bojtor, G. Bognár, G.J. Köteles (Budapest, Hungary)

Fast neutrons action at chromatin level  
L. Radu, B. Constantinescu, I. Radulescu, V. Preoteasa, D. Gazdaru  
(Bucharest, Romania)

Fish-painting applied to late overexposure dose reconstruction: Interest of a non-human primate study  
I. Sorokine-Durm, S. Kolioubaeva, V. Durand, M. Delbos, K.J. Neelis, G. Wagemaker (Fontenay-aux-Roses, France; St. Petersburg, Russia; Rotterdam, Netherlands)

Membrane fluidity as a potential biological dosimeter in case of accidental exposures?  
L. Vincent-Genod, M. Benderitter, A. Berroud, P. Voisin (Fontenay-aux-Roses, France)

Cytogenetic follow-up study in early irradiated victims and its applicability to retrospective biological dosimetry  
Z. Zhang, C. Jin, X. Liu, X. Cheng, C. Ye (Beijing, China)

## **Parallel Session 2a**

### **Lympho-Hematopoietic System**

Chairmen: T.J. MacVittie & B.L. Ziegler

The role of ex vivo expansion in the hemopoietic transplantation of myeloablated recipients  
B. Albella, J.C. Segovia, G. Güenechea, J.A. Bueren (Madrid, Spain)

Ex vivo expansion of hematopoietic cells as a new approach to treatment of accidental irradiation-induced aplasia: potential benefit of modulating radiation- induced apoptosis  
F. Hérodin, M. Drouet, J. Mathieu, N. Grenier, D. Thierry, E. Multon (La Tronche and Fontenay-aux-Roses, France)

Thrombopoietin combined with early-acting growth factors effectively expands human hematopoietic progenitor cells in vitro  
J.-A. Hunnestad, R. Steen, G.E. Tjonnfjord, T. Egeland (Oslo, Norway)

Effect of in vitro on the hematopoietic supportive function of human bone marrow endothelial cells  
M.H. Gaugler, C. Squiban, M.A. Mounthon, M. Vandamme, A. Van Der Meeren (Fontenay-aux-Roses, France)

Seeding-efficiency of human stem cells in NOD/SCID mice: consequences for frequency assessment  
P.B. van Hennik, A.E. de Koning, R.E. Ploemacher (Rotterdam, Netherlands)

Progenitopoietin-G, an engineered chimeric agonist for Flt-3 and G-CSF receptors stimulates multilineage hematopoietic recovery following radiation-induced myelosuppression

A.M. Farese, W.G. Smith, J.P. McKearn, T. MacVittie (Baltimore, MD and St. Louis, MO, USA)

Improvement of survival and hematopoietic recovery with TPO following high doses of  $\gamma$  irradiation

A. Van Der Meeren, M.-H. Gaugler, M.-A. Mounthou, C. Squiban, M. Vandamme, P. Gourmelon, G. Wagemaker (Fontenay-aux-Roses, France; Rotterdam, Netherlands)

15:30 - 17:00

## **Session VI** **Diagnosis And Treatment Of The Cutaneous Syndrome**

Chairmen:

J.W. Hopewell (Oxford, United Kingdom) & M. Martin (Saclay, FR)

Introduction

The skin: its structure and responses to ionizing radiation

J.W. Hopewell

Mechanisms of induction and development of the radiation-induced cutaneous syndrome

M. Martin, C. Geffrotin, M.-C. Vozenin, F. Crechet, Y. Tricaud, S. Delanian, J.-L. Lefaix (Saclay, France)

Diagnosis and treatment of the cutaneous radiation syndrome

R.U. Peter (Ulm, Germany)

Role of chemokines and inflammation

N Lukacs (Ann Arbor, MI, USA)

17:00 - 18:00

## **Poster Session II**

**Topic 7: Diagnosis and treatment of Gastro-Intestinal and Other Acute Organ Damage**

**Topic 8: Follow-Up of Irradiated Persons, Late Organ Damage**

**Topic 9: Protracted or Chronic Exposure**

**Topic 10: Protocol Development**

18:00 - 20:30

**Special Clinical Symposium**

**Growth Factors And Cytokines: Clinical Trials Results  
sponsored By Searle R&D, Monsanto Co., St Louis, MO, USA**

Chairmen: B. Löwenberg (Rotterdam, Netherlands) & C.Schiffer (Detroit, MI, USA)

A perspective on cytokine use  
C. Schiffer

The biology and clinical potential of Flt-3-Ligand  
D.E. Williams (Immunex, Seattle, WA, USA) (Presented by H. McKenna)

Clinical experience with Daniplastim, a synthetic IL-3 receptor agonist  
A. Ganser (Hannover, Germany)

Recombinant human Thrombopoietin (rhTPO) - Clinical development overview

M.C. Benyunes, D.V. Jones Jr, M. Ashby, S. Vadhan-Raj, G. Somlo, R. Champlin, J. Gajewski, S. Hellmann, G. Fyfe (Genentech, South San Francisco, CA, USA)

Clinical trials with megacaryocyte growth and development factor  
J. Crawford, W. Sheridan (Durham, NC, USA)

Novel chimeric cytokines: preclinical and clinical models  
J. DiPersio (St Louis, MO, USA)

Clinical results of IL-11. Why should it be effective  
G. Spitzer (Washington, DC, USA)

**Wednesday, September 2**

08:00 - 10:00

**Session VII**

**Diagnosis And Treatment Of Gastro-Intestinal And Other  
Acute Organ Damage**

Chairpersons:

N.M. Griffiths (Fontenay-aux-Roses, France) & C.S. Potten (Manchester, United Kingdom)

Introduction  
Gastrointestinal radiation induced injury - severity and prognosis  
N.M. Griffiths

Protection against gastrointestinal mucositis by growth factors  
C.S. Potten

Effects of IL-11 in models of gut damage  
D.A. Williams, X. Du (Indianapolis, IN, USA)

The effects of keratinocyte growth factor in preclinical models of mucositis  
C.L. Farrell, K.L. Rex, J.N. Chen, J.V. Bready, C.R. DiPalma, A. Eli, S. Scully, C.S. Potten, D.L. Lacey (Thousand Oaks, CA, USA; Manchester, United Kingdom)

Intestinal Trefoil Factors  
P.L. Beck (Boston, MA, USA)

**10:30 - 12:30 Young Investigators Session**  
Chairmen: P. Gourmelon and G. Wagemaker

Isolation and characterization of a novel DNA repair gene-*pprA*  
Z. Du, I. Narumi, H. Watanabe (Takasaki, Japan)

Diagnostics and non-surgical treatment of cutaneous radiation syndrome in Georgian patients  
P. Gottlöber, G. Bezold, R.U. Peter (Ulm, Germany)

Immune status of children and adolescents with Hashimoto's thyroiditis from the areas contaminated as a result of the Chernobyl accident  
G.S. Molostvov, E.N. Shavrova (Minsk, Belarus)

Betaleukin (rIL-1 $\beta$ ) administered during pancytopenia after autologous transplantation of hematopoietic stem cells  
H. Morozova, S. Ketlinsky, B. Afanasiev (St. Petersburg, Russia)

Modeling change in lymphocyte micronucleus frequencies post cessation of exposure from radioactive buildings in a human population  
M. Tsai, B. Hwang, J. Hwang, W.P. Chang (Taipei, Taiwan)

Regression of radiation-induced fibrosis by superoxide dismutase  
M.-C. Vozenin-Brottons, C. Geffrotin, V. Sivan, Y. Tricaud, N. Gault, S. Delanian, M. Martin, J.-L. Lefaix (Saclay and Paris, France)

Retroviral gene transfer of the enhanced green fluorescent protein gene into human umbilical cord blood cells  
M.M.A. Verstegeen, B.P. van Hennik, M.F.A. Bierhuizen, A.W. Wognum, R.E. Ploemacher, J.A. Cancelas, A. Limón, J. Barquinero, G. Wagemaker (Rotterdam, Netherlands; Barcelona, Spain)

**Parallel Session 2b****Lympho-Hematopoietic System**Chairmen: A. Ganser and M.R. Bishop

Ex vivo expansion of peripheral blood hemopoietic CD34+ cells from normal donors and from an accidentally irradiated patient: engraftment potential of expanded CD34+ cells in NOD/SCID mice

B.L. Ziegler, T. Bock, R. Müller, I. Köhler, A. Otto, T.M. Fliedner (Tübingen and Ulm, Germany )

Irradiation of human thymic stromal cells reduces T cell precursor proliferation: Evidence for a soluble mediator

J.M. Bertho, J. Aigueperse, P. Gourmelon (Fontenay-aux-Roses, France)

Efflux of CD34+ cells from bone marrow to peripheral blood is selective in steady-state haemopoiesis and during granulocyte colony-stimulating factor administration

R. Steen, G.E. Tjonnfjord, L.A. Gunnes, D. Heldal, T. Egeland (Oslo, Norway)

Evaluation of the in vivo hemopoietic potential of stem cells transduced with retroviral vectors expressing the green fluorescent protein as marker

A.W. Wognum, M.F.A. Bierhuizen, T.P. Visser, Y. Westerman, G. Wagemaker (Rotterdam, Netherlands)

**Parallel Session 3****Organ Damage**Chairmen: R.U. Peter and N. Dainiak

Radiation-induced alterations of colonic function in the rat: changes in neural responses and immunocompetent cells

A. François, N.M. Griffiths (Fontenay-aux-Roses, France)

Application of laser doppler flowmetry and ultrasound duplex imaging with color-coded doppler in patients with local radiation injuries consequences

V.G. Leliuk, S.V. Filin (Moscow, Russia)

Modification of early epithelial and late dermal changes in pig skin model

M. Rezvani, E. Whitehouse, L. Frenkel, J. Wilkinson, G. Ross, G. Morris, J.W. Hopewell (Oxford, United Kingdom; Kharkiv, Ukraine)

Colony formation and radiosensitivity in pig epidermis; a new assay based on in situ BrdU-labelling. Possible influence of growth factors

G.J.M.J. van den Aardweg, W.J. Mooi (Rotterdam, Netherlands)

Modification of gut alterations induced after whole-body irradiation by a substance P antagonist in the rat

C. Linard, V. Esposito, J. Wysocki, N.M. Griffiths (Fontenay-aux-Roses, France)

#### **Parallel Session 4**

#### **Follow-Up Of Irradiated Persons**

Chairmen: P. Hall and A. Pinchera

The hematological effects in acute radiation syndrome convalescents (database analysis during 12 years)

V. Bebeshko, A. Kovalenko, D. Belyi, O. Gergel, I. Dyagel (Kiev, Ukraine)

Development of a system for evaluation and archiving of radiation accidents based on case histories: The SEARCH approach

I. Friescke, K. Beyrer, D. Densow, C. Greiner, H. Kindler, R. Wedel, M. Weiss, T.M. Fliedner (Ulm, Germany)

Health status of radiation accident victims at the late consequence period (in-patient observation data)

N.M. Nadejina, I.A. Galstian, V.J. Soloviev, A.A. Savitskey, J.N. Rusheva, J.V. Uvatscheva (Moscow, Russia)

Health and functional status of long-term survivors of the Chernobyl accident

M. Weiss, D. Belyi, O. Gergel, V.A. Bebeshko, N.M. Nadejina, I.A. Galstian, S. Jodi, T.M. Fliedner (Ulm, Germany, Kiev, Ukraine, Moscow, Russia)

The first presumably radiogenic leukemia in Chernobyl area. A case report

B.V. Afanassiev, L.S. Zoubarovskaya, A.B. Chukhlovin, O.V. Marinets, I. Vorobtsova, A. Bogomasova (St. Petersburg, Russia)

Breast cancer rates among women in Belarus prior to and following the Chernobyl catastrophe

V.A. Ostapenko, E.J. Dainiak, E. Sosnovskaya, V. Bruhnov, L.V. Karkanitsa, K. Hunting, N. Dainiak (Mogilev, Belarus; Washington, DC and Bridgeport, CT, USA)

15.00 - 17.30

#### **Session VIII**

#### **Follow-Up Of Irradiated Persons, Late Organ Damage**

Chairmen: J.J. Broerse (Leiden, Netherlands) & N. Wald (Pittsburgh, PA, USA)

Introduction

Late deterministic and stochastic sequelae of ionizing radiation

J.J. Broerse

## Cancer risk in atomic bomb survivors, Update K. Mabuchi (Hiroshima, Japan) (presented by D.A. Pierce)

## Clinical aspects of post-Chernobyl radiation-induced thyroid cancer and thyroid autoimmunity

A. Pinchera, T. Vorontsova, F. Pacini, E. Molinaro, E. Shavrova, L. Agate, E. Kuchinskaya, R. Elisei, E.P. Demidchik (Pisa, Italy; Minsk, Belarus)

## Early effects and late consequences of accidental radiation exposure T.M. Fliedner (Ulm, Germany)

## Registration of radiation accident cases R. Ricks (Oak Ridge, TN, USA)

## Follow-up of acute or subacute radiation sickness patients from radiation accidents in China

G. Ye, S. Huang, G. Wang, S. Shao, B. Liu, C. Jin, H. Wang, B. Fu, R. Min, F. Guo, J. Li, J. Zhang, H. Ai (Beijing, China)

## **20.00 Banquet**

**Thursday, September 3**

8:00 - 10:00

## **Session IX**

# **Protracted Or Chronic Exposure**

Chairmen: T.M. Fliedner (Ulm, Germany) & Ye Gen-Yao (Beijing, China)

### Introduction:

## Protracted or chronic exposure to ionizing radiation: A challenge for radiation accident management

T.M. Fliedner

## Experimental studies on late effects of radiation exposure.

T. Seed, A. Miller, T.E. Fritz (Bethesda, MD and Argonne, IL, USA).

## Late effects of chronic exposure to ionizing radiation

S. Shalaginov, A. Akleyev, P. Hall, (Chelyabinsk, Russia; Stockholm, Sweden)

## Long-term status of immunity and hemopoiesis after chronic radiation exposure of red bone marrow in humans.

A.V. Akleyev, L.A. Silkina, G.A. Veremeyeva, A.V. Vozilova (Chelyabinsk, Russia)

## Health effects of chronic low-dose exposure in human populations Wushou P. Chang (Taipei, Taiwan)

10.30 - 12.00

**Session X**  
**Practical Protocol Development For The Treatment Of Acute  
Radiation Damage**

Chairpersons: J.-M. Cosset & A.E. Baranov (Moscow, Russia)

Introduction:

Pathogenesis and treatment of very severe forms of acute radiation disease in human

A.E. Baranov, A.K. Guskova, M.V. Konchalovsky (Moscow, Russia)

Medical treatment protocol for radiation accident victims as a basis for a computerized guidance system (METREPOL)

T.M. Fliedner (Ulm, Germany)

Management of an acute radiation emergency in Georgia

R.U. Peter (Ulm, Germany)

Dose assessment in the Georgian accident and new therapeutic approach in the treatment of the cutaneous syndrome

P. Gourmelon (Fontenay-aux-Roses, France)

13:00 - 14:30

**Session XI**  
**Conclusions And Consensus**

Chairman : J.C. Nénot (Fontenay-aux-Roses, FR)

Moderators: A.E. Baranov, J.R. Harrison (NRPB, Chilton, Didcot, United Kingdom), T.J. MacVittie, G. Wagemaker

Topics to be considered :

approaches to early diagnosis and triage;

lessons learned from the accidents and the follow-up of over-exposed;  
guidelines for treatment;

guidelines in case of another accident; where are we at?

14:30 - 14:45

**Closing Of The Meeting And Farewell**

15:00 - 17:00

**Satellite Meeting:  
The International Association Of Radiopathology**